CLAIMS

What is claimed is:

1. A method of promoting healing of a chronic dermal skin ulcer on a subject, said method comprising the step of contacting the chronic dermal skin ulcer with an effective amount of an agonist of the non-proteolytically activated thrombin receptor, alone or in combination with an antimicrobial, a disinfectant, an antibiotic, an analgesic or an anti-inflammatory.

2. The method of Claim 1 wherein the chronic dermal skin ulcer is a diabetic ulcer.

3. The method of Claim 1 wherein the chronic dermal skin ulcer is a decubitus ulcer, a venous stasis ulcer or an arterial ulcer.

4. The method of any one of Claims 1 to 3 wherein the agonist is a thrombin peptide derivative.

5. The method of Claim 4 wherein the agonist is a thrombin peptide derivative having the amino acid sequence R1-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2 (SEQ ID NO.: 5),
wherein:
R1 is -H or R3-C(O)-;
R2 is -OH or -NR4R5;
R3 is -H or a C1-C6 alkyl group; and
R4 and R5 are independently -H, a C1-C6 alkyl group or, taken together with the nitrogen atom to which they are bonded, a non-aromatic heterocyclic group;

provided that zero, one, two or three amino acids at positions 1-9 and 14-23 in the thrombin peptide derivative differ from the amino acid at the corresponding position of SEQ ID NO.: 5; an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.

6. The method of Claim 5 wherein R1 is -H and R2 is -NH2.

7. The method of Claim 5 wherein R1 is -H and R2 is -OH.

8. The method of Claim 4 wherein the thrombin peptide derivative has the amino acid sequence R1-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2 (SEQ ID NO.: 5), provided that zero, one, two or three amino acids at positions 1-9 and 14-23 in the thrombin peptide derivative are conservative substitutions of the amino acid at the corresponding position of SEQ ID NO.: 5; an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.

9. The method of Claim 8 wherein R1 is -H and R2 is -NH2.

10. The method of Claim 8 wherein R1 is -H and R2 is -OH.

11. The method of Claim 8 wherein the thrombin peptide derivative has the amino acid sequence R1-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-X1-Gly-Asp-Ser-Gly-Gly-Pro-X2-Val-R2 (SEQ ID NO.: 2), wherein X1 is Glu or Gln and X2 is Phe, Met, Leu, His or Val; or an *N*-terminal truncated

fragment of the thrombin peptide derivative having at least fourteen amino acids; or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.

12. The method of Claim 11 wherein R1 is -H and R2 is -NH2.

13. The method of Claim 11 wherein R1 is -H and R2 is -OH.

14. The method of Claim 11 wherein the thrombin peptide derivative has the amino acid sequence R1-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2 (SEQ ID NO.: 2); an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.

15. The method of Claim 14 wherein R1 is -H and R2 is -NH2.

16. The method of Claim 14 wherein R1 is -H and R2 is -OH.

17. A method of Claim 4 wherein the thrombin peptide derivative has the amino acid sequence H-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-NH2 (SEQ ID NO.: 6).

18. A method of Claim 4 wherein the thrombin peptide derivative has the amino acid sequence R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-Met-Lys-Ser-Pro-Phe-R2 (SEQ ID NO.: 3),
wherein:

R1 is -H or R3-C(O)-;

R2 is -OH or -NR4R5;

R3 is -H or a C1-C6 alkyl group; and

R4 and R5 are independently -H, a C1-C6 alkyl group or, taken together with the nitrogen atom to which they are bonded, a non-aromatic heterocyclic group;

provided that zero, one, two or three amino acids at positions 1-14 and 19-33 of the thrombin peptide derivative differ from the amino acid at the corresponding position of SEQ ID NO.: 3; an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.

19. The method of Claim 18 wherein R1 is -H and R2 is -NH2.

20. The method of Claim 18 wherein R1 is -H and R2 is -OH.

21. The method of Claim 18 wherein the thrombin peptide derivative has the amino acid sequence R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Try-Lys-Pro-Asp-Glu- Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-Met-Lys-Ser- Pro-Phe-R2 (SEQ ID NO.: 3), provided that zero, one, two or three amino acids at positions 1-14 and 19-33 of the thrombin peptide derivative are conservative substitutions of the amino acid at the corresponding position of SEQ ID NO.: 3); an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; or an *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.

22. The method of Claim 18 wherein the thrombin peptide derivative has the amino acid sequence R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Try-Lys-Pro-Asp-Glu-Gly-

Lys-Arg-Gly-Asp-Ala-Cys-X1-Gly-Asp-Ser-Gly-Gly-Pro-X2-Val-Met-Lys-Ser-Pro-Phe-R2 (SEQ ID NO 4), wherein X1 is Glu or Gln and X2 is Phe, Met, Leu, His or Val; an *N*-terminal truncated fragment of the thrombin peptide derivative having at least fourteen amino acids; a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids.

23. The method of Claim 22 wherein R1 is -H and R2 is -NH2.

24. The method of Claim 22 wherein R1 is -H and R2 is -OH.

25. The method of Claim 22 wherein X1 is Glu and X2 is Phe.

26. The method of any one of Claims 1 to 25 wherein the subject is a companion animal, a farm animal or a laboratory animal.

27. A method of promoting healing of a chronic dermal skin ulcer on a subject, said method comprising the step of contacting the chronic dermal skin ulcer with an effective amount of an agonist of the non-proteolytically activated thrombin receptor in the absence of a protease inhibitor agent.